REMARKS

After entry of the amendment, Claims 1-34 are pending in the application. Claims 1, 6, 11, 16, 17, 29, 31, and 33 have been editorially amended and remain supported by the specification. No issues of new matter should arise, and entry of the amendment is respectfully requested.

I. Provisional Non-statutory Obviousness-type Double Patenting Rejections

A. Claims 1-34 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-38 of copending Application No. 10/752,523 in view of Elan Pharma, FDA Approved Labeling Text, pages 1-24 (March 27, 2004).

Applicants respectfully traverse the rejection. A brief exemplary comparison of the claims in the present application to the claims in US Application No. 10/752,523 is set forth below.

Present Application	US Application No. 10/752,523
Adverse events of zonisamide are monoclonal gammopathy of undetermined significance (MGUS), smoldering multiple myeloma (SMM), or multiple myeloma (MM)	Adverse event of zonisamide is rhabdomyolysis

Applicants assert that informing a patient about the adverse event of MGUS, SMM, or MM would not be obvious in view of informing a patient about the adverse event of rhabdomyolysis, as recited in US Application No. 10/752,523. The claims in US Application No. 10/752,523 are directed to informing a patient about rhabdomyolysis, a different disease than that recited in the pending claims.

Elan Pharma, FDA Approved Labeling Text, pages 1-24 (March 27, 2004) does not cure the deficiencies of US Application No. 10/752,523. Neither the primary nor the secondary references mention MGUS, SMM, MM, or rhabdomyolysis as an adverse event.

In view of the above, Applicants respectfully request that this provisional obviousness-type double patenting rejection be withdrawn.

B. Claims 1-34 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-41 of copending Application No. 10/752,522 (published as 2005/0154033).

Applicants respectfully traverse the rejection. A brief exemplary comparison of the claims in the present application to exemplary claims in of US Application No. 10/752,522 is set forth below.

Present Application	US Application No. 10/752,522
Adverse events of zonisamide are monoclonal gammopathy of undetermined significance (MGUS), smoldering multiple myeloma (SMM), or multiple myeloma (MM)	Adverse event of zonisamide is NMS [neuroleptic malignant syndrome]

Applicants assert that informing a patient about the adverse event of MGUS, SMM, or MM would not be obvious in view of informing a patient about the adverse event of neuroleptic malignant syndrome (i.e., NMS), as recited in US Application No. 10/752,522. The claims in US Application No. 10/752,522 are directed to informing a patient about neuroleptic malignant syndrome (i.e., NMS), a different disease than that recited in the pending claims.

In view of the above, Applicants respectfully request that this provisional obviousness-type double patenting rejection be withdrawn.

C. Claims 1-34 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting over (i) claims 1-15 of copending Application No. 10/644,935; (ii) claims 1-36 of copending Application No. 10/752,516; (iii) claims 1-39 of copending US Application No. 10/753,957; (iv) claims 1-36 of copending Application No. 10/752,515.

Applicants respectfully traverse each of the four rejections for the reasons stated below.

(i) US Application No. 10/644,935 (published as 2005/0043773)

A brief comparison of exemplary claims in the present application to exemplary claims in US Application No. 10/644,935 is set forth below.

Present Application	US Application No. 10/644,935
Adverse events of zonisamide are monoclonal gammopathy of undetermined significance (MGUS), smoldering multiple myeloma (SMM), or multiple myeloma (MM)	Adverse events of zonisamide are abdominal pain, hypovolemia, shock, nausea, anorexia, vomiting, and abdominal distention

Applicants assert that informing a patient about the adverse event of MGUS, SMM, or MM would not be obvious in view of informing a patient about the adverse events of abdominal pain, hypovolemia, shock, nausea, anorexia, vomiting, and abdominal distention, as recited in US Application No. 10/644,935.

In view of the above, Applicants respectfully request that this provisional obviousness-type double patenting rejection be withdrawn.

(ii) US Application No. 10/752,516 (published as 2005/ 0154032)

A brief comparison of exemplary claims in the present application to exemplary claims in US Application No. 10/752,516 is set forth below.

Claim 1 of Present Application	US Application No. 10/752,516
Adverse events of zonisamide are monoclonal gammopathy of undetermined significance (MGUS), smoldering multiple myeloma (SMM), or multiple myeloma (MM)	Averse event of zonisamide is hyperammonemia

Applicants assert that informing a patient about the adverse event of MGUS, SMM, or MM would not be obvious in view of informing a patient about the adverse event of hyperammonemia, as recited in US Application No. 10/752,516. The claims in US Application

No. 10/752,516 are directed to informing a patient about hyperammonemia, a different disease than that recited in the pending claims.

In view of the above, Applicants respectfully request that this provisional obviousness-type double patenting rejection be withdrawn.

(iii) US Application No. 10/753,957 (published as 2005/0043705)

A brief comparison of exemplary claims in the present application to exemplary claims in US Application No. 10/753,957 is set forth below.

Claim 1 of Present Application	US Application No. 10/753,957
Adverse events of zonisamide are monoclonal gammopathy of undetermined significance (MGUS), smoldering multiple myeloma (SMM), or multiple myeloma (MM)	Adverse event of zonisamide is pancreatitis.

Applicants assert that informing a patient about the adverse event of MGUS, SMM, or MM would not be obvious in view of informing a patient about the adverse event of pancreatitis, as recited in US Application No. 10/753,957. The claims in US Application No. 10/753,957 are directed to informing a patient about pancreatitis, a different disease than that recited in the pending claims.

In view of the above, Applicants respectfully request that this provisional obviousness-type double patenting rejection be withdrawn.

(iv) US Application No. 10/752,515 (published as 2005/0043704)

A brief comparison of exemplary claims in the present application to exemplary claims in US Application No. 10/752,515 is set forth below.

Claim 1 of Present Application	Claim 1 of US Application No. 10/752,515
Adverse events of zonisamide are monoclonal gammopathy of undetermined significance (MGUS), smoldering multiple myeloma (SMM), or multiple myeloma (MM)	Adverse event of zonisamide is **pancreatitis**.

Applicants assert that informing a patient about the adverse event of MGUS, SMM, or MM would not be obvious in view of informing a patient about the adverse event of pancreatitis, as recited in US Application No. 10/752,515. The claims in US Application No. 10/752,515 are directed to informing a patient about pancreatitis, a different disease than that recited in the pending claims.

In view of the above, Applicants respectfully request that this provisional obviousness-type double patenting rejection be withdrawn.

D. In the first full paragraph on page 7 of the Office Action, it is suggested that Applicants should review all their issued patents and pending applications and submit appropriate Terminal Disclaimers. The PTO then cites US Application Nos. 10/753,955 and 10/753,956 as examples.

(i) US Application No. 10/753,955 (published as 2005/0154035)

A brief comparison of exemplary claims in the present application to exemplary claims in US Application No. 10/753,955 is set forth below.

Claim 1 of Present Application	Application No. 10/753,955
Adverse events of zonisamide are monoclonal gammopathy of undetermined significance (MGUS), smoldering multiple myeloma (SMM), or multiple myeloma (MM)	Adverse event of zonisamide is rhabdomyolysis

Applicants assert that informing a patient about the adverse event of MGUS, SMM, or MM would not be obvious in view of informing a patient about the adverse event of rhabdomyolysis, as recited in US Application No. 10/753,955. The claims in US Application No. 10/753,955 are directed to informing a patient about rhabdomyolysis, a different disease than that recited in the pending claims.

(ii) US Application No. 10/753,956 (published as 2005/0154036)

A brief comparison of exemplary claims in the present application to exemplary claims in US Application No. 10/753,956 is set forth below.

Present Application	US Application No. 10/753,956
Adverse events of zonisamide are monoclonal gammopathy of undetermined significance (MGUS), smoldering multiple myeloma (SMM), or multiple myeloma (MM)	Adverse event is hyperammonemia

Applicants assert that informing a patient about the adverse event of MGUS, SMM, or MM would not be obvious in view of informing a patient about the adverse event of hyperammonemia, as recited in US Application No. 10/753,956. The claims in US Application No. 10/753,956 are directed to informing a patient about hyperammonemia, a different disease than that recited in the pending claims.

II. Rejection under 35 U.S.C. § 112, second paragraph, indefiniteness

A. Claims 1-15 are rejected under 35 U.S.C. § 112, second paragraph, indefiniteness, for reciting "such therapy" in independent claims 1, 6 and 11. The Office Action states that it is unclear what the term specifically relates to, and that is could reasonably be interpreted to related back to adjunctive therapy, or non-adjunctive therapy, in view of the dictionary definition of the term "adjunct."

Applicants have amended claims 1, 6 and 11 as suggested by the Examiner, replacing "such therapy" with "said adjunctive therapy," to advance the prosecution of this application.

Applicants assert that the term "adjunctive therapy" (rather than "adjunct") is well known in the art. Applicants further refer to the specification at paragraph [0028] of the published application, which exemplifies the definition known in the art: "Adjunctive therapy for partial seizures in adults denotes that these patients are already on other anti-epileptic medications, but that they are continuing to seize at a rate that has been deemed by their treating physician to require additional (add-on) therapy."

In light of the claim amendments and remarks, it is respectfully requested that this rejection of claims 1-15 under 35 U.S.C. § 112, second paragraph, be withdrawn.

B. Claims 1-15 are rejected under 35 U.S.C. § 112, second paragraph, indefiniteness, as omitting matter disclosed to be essential to the invention in independent claims 1, 6 and 11. The Office Action states that the steps of "providing a patient with a therapeutically effective amount of zonisamide" and the step of "informing the patient or the patient's guardian during the course of zonisamide therapy" are not specifically related to "prompt medical evaluation," which is considered essential for practicing the claimed method.

Applicants have editorially amended claims 1, 6 and 11 to highlight the third step, in which the patient or the patient's guardian is informed that monoclonal gammopathy of undetermined significance (MGUS), smoldering multiple myeloma (SMM), or multiple myeloma (MM) require prompt medical evaluation. The patient or the patient's guardian must be informed about the adverse events of taking zonisamide in case they experience the adverse events, at which time they should seek prompt medical evaluation.

It is therefore respectfully requested that this rejection of claims 1-15 under 35 U.S.C. § 112, second paragraph, be withdrawn.

C. Claim 1 is rejected under 35 U.S.C. § 112, second paragraph, indefiniteness, pointing to a possible typographical error amongst the terms "increased frequency or duration of infection" and "odor are symptoms." Applicants have amended claim 1 to replace "or" with "and" between these terms. Therefore it is respectfully requested that this rejection of claim 1 under 35 U.S.C. § 112, second paragraph, indefiniteness, be withdrawn.

III. Rejection under 35 U.S.C. § 112, first paragraph, enablement

Claims 1-34 are rejected under 35 U.S.C. § 112, first paragraph, enablement. Applicants provide a further discussion of the *Wands* factors below.

1. The relative skill of those in the art. With respect to the level of skill in the art, page 10 in the Office Action states that the relative skill of those in the art is high, generally that of an

M.D. or Ph.D. Applicants agree, and this factor thus weighs heavily in favor of Applicants.

2. The nature of the invention. The claimed invention is directed, *inter alia*, to identifying that zonisamide may result in an adverse event of MGUS, SMM or MM, and to informing of the symptoms of the same. Based on the disclosures in the present application, the skilled artisan would recognize that the recited symptoms may indicate MGUS, SMM or MM. Moreover, it is routine practice for the skilled worker, e.g., a medical doctor, to consider a patient's symptoms, prescription/OTC medications, and other illnesses when making a diagnosis. Routine experimentation is all that is necessary to make an appropriate diagnosis based on the teachings and claims in the present application. A person highly skilled in the art is able to evaluate the patient in order to determine the cause of the patient's symptoms.

Having the knowledge that MGUS, SMM, and MM are adverse events associated with zonisamide (as described in the present application), and the knowledge of the symptoms of MGUS, SMM, and MM (as described in the present application), a person skilled in the art (e.g., M.D. or Ph.D.) can routinely determine if a patient taking zonisamide is experiencing an adverse event (e.g., MGUS, SMM, MM) that requires prompt medical attention.

An prescribing physician, in particular, routinely deals with diagnosing diseases and adverse drug events. With the knowledge of the teachings of the claimed invention (for example, patient taking zonisamide; MGUS, SMM, MM may be adverse events of zonisamide; symptoms of MGUS, SMM, MM), an M.D. could use routine experimentation (e.g., routine lab tests) to determine whether a patient on zonisamide is experiencing the adverse events of MGUS, SMM, or MM. The routine experiments may reveal that the patient does not have MGUS, SMM, or MM.

Therefore this factor also weighs in favor of Applicants.

3. The state and predictability of the art. In the Office Action at pages 11-13, the PTO summarizes the following references: Asai et al, *Internal Medicine*, 41(2):138-141 (2002); Kyle, *Clin. Chem.*, 40/11(B):2154-2161 (1994); and Fujimoto, Arzmeim-Forsch/Drug Res., 40(11):855-858, No. 8 (1990). It is unclear to Applicants what conclusion is drawn from these reference summaries.

In particular, to the extent that the Examiner may be relying on Asai et al, *Internal Medicine*, 41(2):138-141 (2002) to support this enablement rejection, Applicants respectfully note that the Examiner also relies on Asai to support an obviousness rejection. *See* Office Action at pages 20-21. Moreover, it appears that one of the positions taken is that Asai merely provides anecdotal reports of zonisamide-induced SMM. *See* Office Action at page 14, lines 15-19; specification at Example 1. Each of these positions contradicts the others. Applicants respectfully request clarification of the PTO's interpretation of Asai.

4. **The breadth of the claims.** The Office Action states on Page 13 that other therapies are included in the recitation of "improve the safety of such therapy." Applicants assert that the claims are directed to the use of zonisamide as adjunctive therapy, that the term "adjunctive therapy" (rather than "adjunct") is known in the art, and exemplified by the following description at paragraph [0028] of the published application: "Adjunctive therapy for partial seizures in adults denotes that these patients are already on other anti-epileptic medications, but that they are continuing to seize at a rate that has been deemed by their treating physician to require additional (add-on) therapy."

Further, any reasonable means of informing the patient or the patient's guardian may be employed, and it is well within the skill of the art to select the appropriate means of communication. For example, and only as illustration, they could inform a patient or patient's guardian by talking to the patient in person; sending a letter to the patient; calling the patient on the telephone and speaking to the patient or leaving a voice message; sending an e-mail to the patient; sending a text message to the patient; sending a facsimile to the patient, etc.

The Office Action goes on to state that the term "informing the patient or the patient's guardian during the course of zonisamide therapy" could reasonably be construed to mean 1 day, or 1 month, or 1 year, or 60 years after the initiation of zonisamide therapy, which would seriously diminish the level of predictability in practicing the claimed invention. However, the skilled artisan would readily understand that an adverse event could occur throughout the course of zonisamide therapy, and thus informing that these symptoms require prompt medical evaluation is useful at any point during the course of zonisamide therapy.

The dosages and decision to cease zonisamide therapy is within the skill of those in the art. In addition, a possible question of the safety and efficacy of zonisamide in children under 16 years of age does not negate the usefulness of informing a patient who is under 16 years of age of these possible symptoms of MGUS, SMM or MM during the course of zonisamide therapy.

5. The nature of the invention. The claimed invention is directed, *inter alia*, to identifying that zonisamide may result in an adverse event of MGUS, SMM or MM, and to identifying the symptoms of the adverse event. The skilled artisan would recognize that the recited symptoms may indicate MGUS, SMM or MM. Moreover, it is routine practice for the skilled worker, e.g., a medical doctor, to consider a patient's symptoms, prescription/OTC medications, and other illnesses when making a diagnosis. Routine testing is all that is necessary to make an appropriate diagnosis based on the teachings and claims in the present application. A person skilled in the art is able to evaluate the patient in order to determine the cause of the patient's symptoms. A skilled person would appreciate knowing what adverse events may occur for zonisamide therapy and would be able to inform regarding what adverse events may occur during the course of treatment.

With respect to the correlation between the dosage of zonisamide and the development of MGUS, SMM, or MM, Applicants respectfully submit that a correlation between a particular dosage of zonisamide and the development of MGUS, SMM, or MM is not necessary to practice the claimed invention. The claims of the invention are directed, *inter alia*, to informing a person of the potential adverse events of MGUS, SMM, or MM that may be associated with zonisamide therapy.

Applicants respectfully submit that the term "prompt medical evaluation" is related to the onset of MGUS, SMM, or MM and the symptoms related to MGUS, SMM, or MM. Accordingly, it is reasonable that a highly skilled person would recognize that prompt medical evaluation may be required at any time during the course of zonisamide treatment, and that prompt medical evaluation would be necessary when an adverse event occurs.

Therefore this factor also weighs in favor of Applicants.

6. The amount of direction or guidance provided and the presence or absence of working examples. Applicants' specification provides direction and guidance regarding the risk

of patients undergoing therapy that includes zonisamide for developing MGUS, SMM or MM, and provides symptoms of these to inform the patient of this risk.

The presence of working examples is not required to satisfy the enablement requirement. *In re Strahilevtz*, 212 USPQ 561, 563 (CCPA 1982). Applicants respectfully assert that one of skill in the art can practice the recited steps recited in the claims without reference to working examples.

Because the specification provides adequate direction and guidance to the skilled artisan, this factor weighs in favor of Applicants.

7. **The quantity of experimentation necessary.** As discussed, undue experimentation would not be necessary for one of skill in the art to practice the claimed methods comprising the steps of providing a therapeutically effective amount of zonisamide, a known adjunct therapy, and informing as detailed in the pending claims. This factor also weighs in favor of Applicants.

8. **Summary.** The combined weight of the *Wands* factors discussed above are in favor of Applicants. Therefore, *there is no reason to doubt* that enablement is satisfied for the claimed methods. See M.P.E.P. § 2164.04. Accordingly, Applicants respectfully request that the rejection of claims 1-34 under 35 U.S.C. § 112, first paragraph, enablement, be withdrawn.

IV. Rejection under 35 U.S.C. § 112, first paragraph, written description

Claims 1-34 are rejected under 35 U.S.C. § 112, first paragraph, written description. The Office Action states in the paragraph spanning Pages 15-16:

> [W]hile the specification provides written description for a method of using zonisamide as an adjunctive therapy for partial seizures to improve the safety of zonisamide i.e. zonisamide-induced adverse effects, including MGUS, it does not reasonably provide written description for a method to improve the safety profile of other concomitant drugs, for example, phenytoin, phenobarbital, or primidone, which are also associated with causing identical/similar adverse effects, such as e.g. phenytoi-induced multiple myeloma.

Applicants respectfully assert that each of the pending claims involve zonisamide therapy, and as such, are not directed to improving the safety profile of other drugs. Therefore, it

is respectfully requested that the rejection of claims 1-34 are rejected under 35 U.S.C. § 112, first paragraph, written description, be withdrawn.

V. Rejection under 35 U.S.C. § 102(b)

Claims 1-15 are rejected under 35 USC § 102(b) as anticipated by Elan Pharma, Zonisamide Approvable Labeling (March 27, 2000) (hereafter "Elan"). Applicants respectfully traverse the rejection.

Anticipation under this section requires that each and every recitation of the claim be found in a single prior art reference. *W. L. Gore & Associates Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1554, 220 U.S.P.Q. 303, 313 (Fed. Cir. 1983). A finding of anticipation further requires that there be no difference between the claimed invention and the disclosure of the cited reference as viewed by one of ordinary skill in the art. *Scripps Clinic & Research Foundation v. Genentech Inc.*, 927 F.2d 1565, 1576, 18 U.S.P.Q.2d 1001, 1010 (Fed. Cir. 1991).

Elan does not explicitly or implicitly recite or refer to the adverse event of MGUS, SMM, or MM that may be caused by zonisamide. Elan does not provide any teaching or suggestion of any symptoms that would be associated with the adverse event of MGUS, SMM, or MM. At pages 16-19, Elan mentions:

- about 34 side effects that occurred in at least 2% of patients treated with zonisamide;
- about 13 sides effects that occurred in at least 1% of patients treated with zonisamide;
- about 82 side effects that occurred in 1% to 0.1% of patients treated with zonisamide; and
- about 42 side effects that occurred in less than 0.1% of patients treated with zonisamide.

Specifically, Elan does not provide any relationship or link between any of the 171 possible side effects described therein with any of the 8-10 symptoms associated with the adverse event of MGUS, SMM, or MM.

Elan does not explicitly or implicitly recite or suggest (i) informing a patient or patient's guardian that zonisamide may cause an adverse event of MGUS, SMM, or MM; (ii) informing a patient or patient's guardian of the symptoms associated with the adverse event of MGUS, SMM, or MM; or (iii) informing a patient that prompt medical evaluation is required for the adverse event of MGUS, SMM, or MM.

In view of the fact that Elan does not teach, or even suggest, each and every element of the claimed invention, Elan cannot anticipate the claimed invention under this section. In view thereof, Applicants respectfully request that the rejection of claims 1-15 under 35 U.S.C. § 102(b) be withdrawn.

VI. Rejection under 35 USC § 103

Claims 16-34 are rejected under 35 U.S.C. § 103 as obvious over Elan Pharma, Zonisamide Approvable Labeling (March 27, 2000) (hereafter "Elan") in view of Asai et al, *Internal Medicine*, 41(2):138-141 (2002) (hereafter "Asai") and further in view of Kyle, *Clin. Chem.*, 40/11(B):2154-2161 (1994) (hereafter "Kyle").

To establish a *prima facie* case of obviousness, three requirements must be satisfied (M.P.E.P. § 2143). First, the prior art relied upon, coupled with the knowledge generally available in the art at the time of the invention, must contain some suggestion or incentive that would have motivated the skilled artisan to modify a reference or to combine references. *In re Oetiker,* 24 U.S.P.Q.2d 1443, 1446 (Fed. Cir. 1992); *In re Fine*, 837 F.2d at 1074; *In re Skinner*, 2 U.S.P.Q.2d 1788, 1790 (Bd. Pat. App. & Int. 1986). Second, the proposed modification or combination of the prior art must have a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *See Amgen, Inc. v. Chugai Pharm. Co.*, 927 F2d 1200, 1209, 18 U.S.P.Q.2d 1016, 1023 (Fed. Cir. 1991). Finally, the prior art reference or combination of references must teach or suggest all of the limitations of the claims. *See In re Wilson* 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (CCPA 1970) ("All words in a claim must be considered in judging the patentability of that claim against the prior art").

Further, the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both come from the prior art, not from Applicants' disclosure. *See In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991); M.P.E.P. § 2143.

Elan does not explicitly or implicitly recite or refer to the adverse event of MGUS, SMM, or MM that may be caused by zonisamide. Elan does not provide any teaching or suggestion of

any symptoms that would be associated with the adverse event of MGUS, SMM, or MM. At pages 16-19, Elan teaches:

- about 34 side effects that occurred in at least 2% of patients treated with zonisamide;
- about 13 sides effects that occurred in at least 1% of patients treated with zonisamide;
- about 82 side effects that occurred in 1% to 0.1% of patients treated with zonisamide; and
- about 42 side effects that occurred in less than 0.1% of patients treated with zonisamide.

Elan does not provide any relationship or link between any of the 171 possible side effects described therein with any of the 8-10 symptoms associated with the adverse event of MGUS, SMM, or MM.

To the extent that the PTO may be relying on Asai et al, *Internal Medicine*, 41(2):138-141 (2002) to support the obviousness rejection, Applicants respectfully note that the Examiner also appears to rely on Asai to support a nonenablement rejection. *See* Office Action at pages 11-12. Moreover, the Examiner states that Asai merely provides anecdotal reports of zonisamide-induced SMM. *See* Office Action at page 14, lines 15-19; specification at Example 1. Each of these positions contradicts the others. If Asai is not an enabling disclosure, then it cannot serve as the basis for an obviousness rejection. Applicants respectfully request clarification of the PTO's interpretation of Asai.

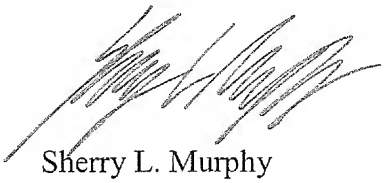
Kyle does not cure the deficiencies of Elan or Asai. Kyle is a review paper concerning monoclonal gammopathies that discusses methods for analyzing serum proteins and providing a differential diagnosis of monoclonal gammopathies. Kyle does not indicate whether the development and testing of the monoclonal gammopathies has any relation to naturally occurring monoclonal gammopathies or to drug-induced adverse events of monoclonal gammopathies. More particularly, Kyle does not provide any teaching or evidence that monoclonal gammopathies may be an adverse event/disease associated with zonisamide. The relationship between the adverse event and the drug is critical information (only described and claimed in the present application) that Kyle does not provide.

In view of the above, Applicants respectfully submit that the claims are unobvious over the combination of cited references, and respectfully request that the rejection of claims 16-34 under § 103 be withdrawn.

VII. Conclusion

An early and favorable reconsideration and allowance of Claims 1-34 is respectfully requested.

Respectfully submitted,



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